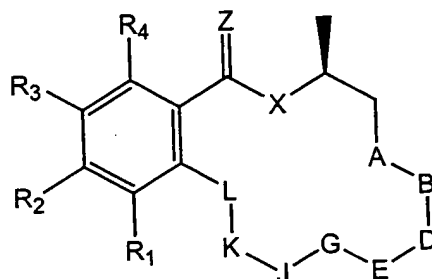


CLAIMS

What is claimed is:

1. A compound having the structure:



wherein

R_1 is hydrogen, halogen, cyano, $-OR_A$, $-N(R_A)_2$, $-SR_A$, $-O(C=O)R_A$, $-N(R_A)(C=O)(R_A)$, $-C(O)R_A$, $-C(O)OR_A$, $-CON(R_A)_2$, $-OCO_2R_A$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_A is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

R_2 is hydrogen, halogen, cyano, $-OR_B$, $-N(R_B)_2$, $-SR_B$, $-O(C=O)R_B$, $-N(R_B)(C=O)(R_B)$, $-C(O)R_B$, $-C(O)OR_B$, $-CON(R_B)_2$, $-OCO_2R_B$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_B is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

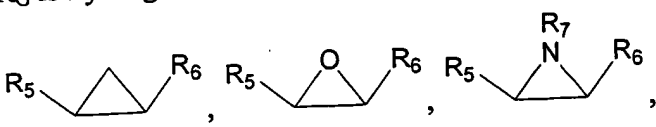
R_3 is hydrogen, halogen, cyano, $-OR_C$, $-N(R_C)_2$, $-SR_C$, $-O(C=O)R_C$, $-N(R_C)(C=O)(R_C)$, $-C(O)R_C$, $-C(O)OR_C$, $-CON(R_C)_2$, $-OCO_2R_C$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_C is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

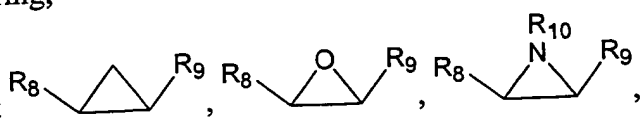
R_4 is hydrogen, halogen, cyano, $-OR_D$, $-N(R_D)_2$, $-SR_D$, $-O(C=O)R_D$, $-N(R_D)(C=O)(R_D)$, $-C(O)R_D$, $-C(O)OR_D$, $-CON(R_D)_2$, $-OCO_2R_D$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, a

1 protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl
2 moiety;

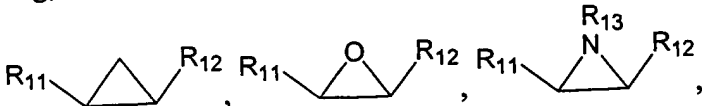
3 Z is O, S, or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic,
4 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is
5 hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
6 alkylheteroaryl moiety;

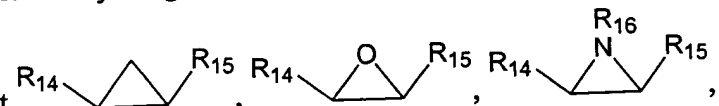
7 X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

8 A and B together represent ,
9 -CHR₅-CHR₆-, -CR₅=CR₆-, wherein R₅ and R₆ are each independently hydrogen, halogen,
10 cyano, -OR_J, -N(R_J)₂, -SR_J, -O(C=O)R_J, -O(S=O)R_J, -N(R_J)(C=O)(R_J), -C(=O)R_J, -C(=O)OR_J,
11 -CON(R_J)₂, -OCO₂R_J, -OS(=O)OR_J or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
12 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
13 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
14 wherein R₇ is hydrogen, a protecting group, -OR_K, -SR_K, -C(O)OR_K, -C(O)NR_K, -S(O)₂R_K, -
15 O(C=O)R_K, -N(R_K)(C=O)(R_K), -C(O)R_K, -C(O)OR_K, -CON(R_K)₂, -OCO₂R_K, or an aliphatic,
16 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
17 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
18 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent -CHR₅-
19 CHR₆-, R₅ and R₆ taken together represent a substituted or unsubstituted 3-7 membered aliphatic,
20 heteroaliphatic, aryl or heteroaryl ring;

21 D and E together represent ,
22 -CHR₈-CHR₉-, -CR₈=CR₉-, wherein R₈ and R₉ are each independently hydrogen, halogen,
23 cyano, -OR_J, -N(R_J)₂, -SR_J, -O(C=O)R_J, -O(S=O)R_J, -N(R_J)(C=O)(R_J), -C(=O)R_J, -C(=O)OR_J,
24 -CON(R_J)₂, -OCO₂R_J, -OS(=O)OR_J or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
25 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
26 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
27 wherein R₁₀ is hydrogen, a protecting group, -OR_K, -SR_K, -C(O)OR_K, -C(O)NR_K, -S(O)₂R_K, -
28 O(C=O)R_K, -N(R_K)(C=O)(R_K), -C(O)R_K, -C(O)OR_K, -CON(R_K)₂, -OCO₂R_K, or an aliphatic,
29 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of

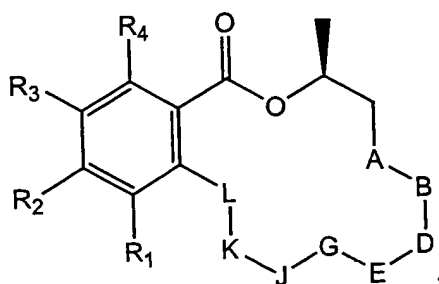
1 R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
 2 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-\text{CHR}_8-$
 3 CHR_9- , R_9 and R_9 taken together represent a substituted or unsubstituted 3-7 membered aliphatic,
 4 heteroaliphatic, aryl or heteroaryl ring;

5 G and J together represent ,
 6 $-\text{CHR}_{11}-\text{CHR}_{12}-$, $-\text{CR}_{11}=\text{CR}_{12}-$, wherein R_{11} and R_{12} are each independently hydrogen, halogen,
 7 cyano, $-\text{OR}_J$, $-\text{N}(\text{R}_J)_2$, $-\text{SR}_J$, $-\text{O}(\text{C}=\text{O})\text{R}_J$, $-\text{O}(\text{S}=\text{O})\text{R}_J$, $-\text{N}(\text{R}_J)(\text{C}=\text{O})(\text{R}_J)$, $-\text{C}(=\text{O})\text{R}_J$, $-\text{C}(=\text{O})\text{OR}_J$,
 8 $-\text{CON}(\text{R}_J)_2$, $-\text{OCO}_2\text{R}_J$, $-\text{OS}(=\text{O})\text{OR}_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
 9 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
 10 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
 11 wherein R_{13} is hydrogen, a protecting group, $-\text{OR}_K$, $-\text{SR}_K$, $-\text{C}(\text{O})\text{OR}_K$, $-\text{C}(\text{O})\text{NR}_K$, $-\text{S}(\text{O})_2\text{R}_K$, $-\text{O}(\text{C}=\text{O})\text{R}_K$,
 12 $-\text{N}(\text{R}_K)(\text{C}=\text{O})(\text{R}_K)$, $-\text{C}(\text{O})\text{R}_K$, $-\text{C}(\text{O})\text{OR}_K$, $-\text{CON}(\text{R}_K)_2$, $-\text{OCO}_2\text{R}_K$, or an aliphatic,
 13 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
 14 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
 15 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-\text{CHR}_{11}-$
 16 $\text{CHR}_{12}-$, R_{11} and R_{12} taken together represent a substituted or unsubstituted 3-7 membered
 17 aliphatic, heteroaliphatic, aryl or heteroaryl ring;

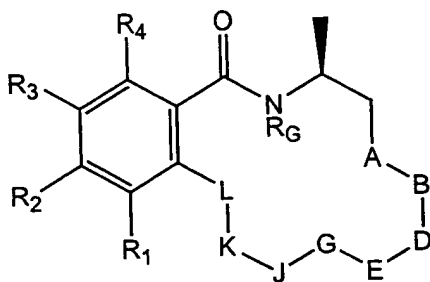
18 K and L together represent ,
 19 $-\text{CHR}_{14}-\text{CHR}_{15}-$, $-\text{CR}_{14}=\text{CR}_{15}-$, wherein R_{14} and R_{15} are each independently hydrogen, halogen,
 20 cyano, $-\text{OR}_J$, $-\text{N}(\text{R}_J)_2$, $-\text{SR}_J$, $-\text{O}(\text{C}=\text{O})\text{R}_J$, $-\text{O}(\text{S}=\text{O})\text{R}_J$, $-\text{N}(\text{R}_J)(\text{C}=\text{O})(\text{R}_J)$, $-\text{C}(=\text{O})\text{R}_J$, $-\text{C}(=\text{O})\text{OR}_J$,
 21 $-\text{CON}(\text{R}_J)_2$, $-\text{OCO}_2\text{R}_J$, $-\text{OS}(=\text{O})\text{OR}_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
 22 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
 23 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
 24 wherein R_{16} is hydrogen, a protecting group, $-\text{OR}_K$, $-\text{SR}_K$, $-\text{C}(\text{O})\text{OR}_K$, $-\text{C}(\text{O})\text{NR}_K$, $-\text{S}(\text{O})_2\text{R}_K$, $-\text{O}(\text{C}=\text{O})\text{R}_K$,
 25 $-\text{N}(\text{R}_K)(\text{C}=\text{O})(\text{R}_K)$, $-\text{C}(\text{O})\text{R}_K$, $-\text{C}(\text{O})\text{OR}_K$, $-\text{CON}(\text{R}_K)_2$, $-\text{OCO}_2\text{R}_K$, or an aliphatic,
 26 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
 27 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
 28 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-\text{CHR}_{14}-$

1 CHR₁₅-, R₁₄ and R₁₅ taken together represent a substituted or unsubstituted 3-7 membered
 2 aliphatic, heteroaliphatic, aryl or heteroaryl ring;
 3 whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently
 4 be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl,
 5 heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted; and
 6 pharmaceutically acceptable derivatives thereof.

7
 8 2. The compound of claim 1, wherein Z and X are each O, and the compound has the
 9 structure:

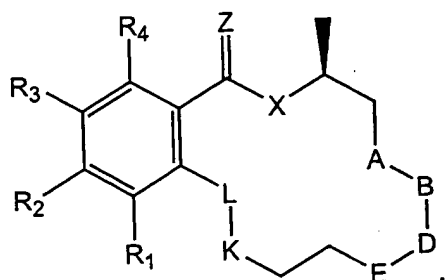


11
 12
 13 3. The compound of claim 1, wherein Z is O and X is NR_G, and the compound has the
 14 structure:

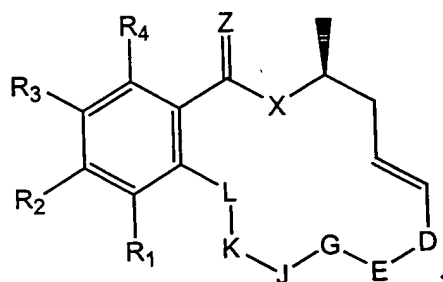


15
 16
 17 4. The compound of claim 3, wherein R_G is H.

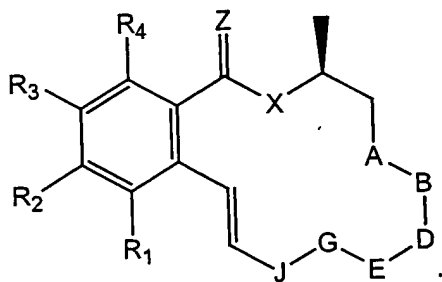
18
 19 5. The compound of claim 1, wherein G and J together represent -CH₂-CH₂- and the
 20 compound has the structure:



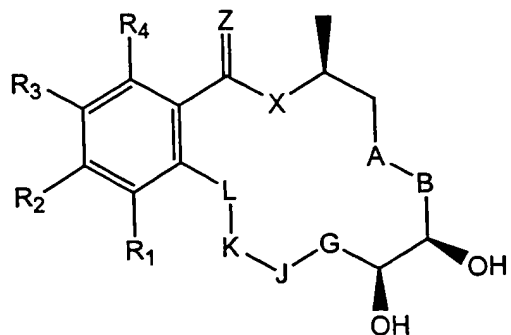
6. The compound of claim 1, wherein A-B is $-\text{CH}=\text{CH}-$ and the compound has the structure:



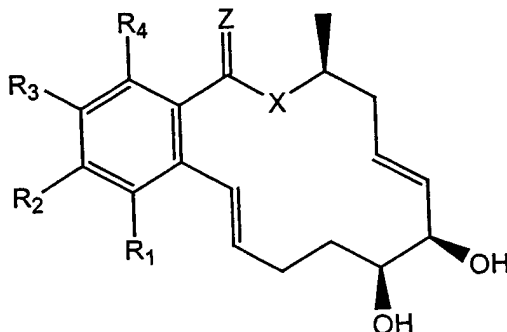
7. The compound of claim 1, wherein K and L together represent $-\text{CH}=\text{CH}-$ and the compound has the structure:



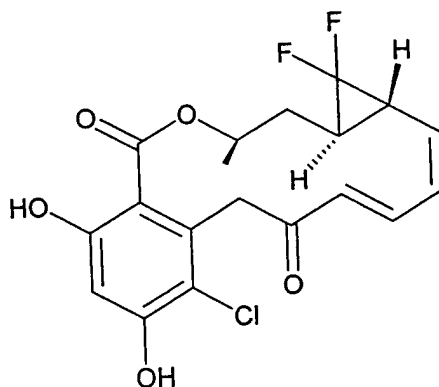
8. The compound of claim 1, wherein D and E together represent $-\text{CHOH}=\text{CHOH}-$ and the compound has the structure:



1
2 9. The compound of claim 1, wherein A, B, D, E, G, J, K, and L are as represented in the
3 structure:



4
5
6 10. A compound of structure:



7
8
9 11. A pharmaceutical composition comprising a compound of claim 1 and a
10 pharmaceutically acceptable carrier.

11
12 12. The pharmaceutical composition of claim 11, further comprising one or more additional
13 therapeutic agents.

14
15 13. The pharmaceutical composition of claim 12, wherein the one or more additional
16 therapeutic agents comprises an anticancer agent.

17
18 14. A method for treating cancer comprising:
19 administering a therapeutically effective amount of a compound of claim 1 to a subject in
20 need thereof.

1
2 15. The method of claim 14, wherein the therapeutically effective amount is in the range of
3 0.001 mg/kg to 50 mg/kg of body weight.

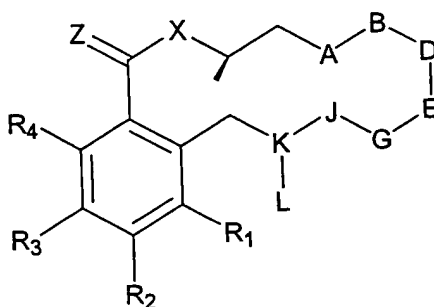
4
5 16. The method of claim 14, wherein the therapeutically effective amount is in the range of
6 0.01 mg/kg to about 25 mg/kg of body weight.

7
8 17. The method of claim 14, said method further comprising administering one or more
9 additional therapeutic agents in combination with the compound.

10
11 18. The method of claim 17, wherein the one or more additional therapeutic agents comprises
12 an anticancer agent.

13
14 19. A method for inhibiting the growth of or killing cancer cells, said method comprising:
15 contacting the cancer cells with an amount of a compound of claim 1 effective to inhibit
16 the growth of or kill cancer cells.

17
18 20. A method for the synthesis of a compound having the structure (I):



(I)

20
21
22 wherein

23 R_1 is hydrogen, halogen, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
24 alkylheteroaryl moiety, or $N(R_A)_2$, wherein each occurrence of R_A is independently hydrogen, a
25 protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl
26 moiety;

27 R_2 is hydrogen, halogen, cyano, $-OR_B$, $-N(R_B)_2$, $-SR_B$, $-O(C=O)R_B$, $-N(R_B)(C=O)(R_B)$,

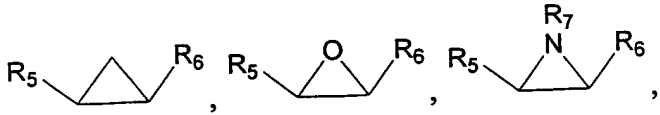
1 -C(O)R_B, -C(O)OR_B, -CON(R_B)₂, -OCO₂R_B, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
2 alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_B is independently hydrogen, a
3 protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl
4 moiety;

5 R₃ is hydrogen, halogen, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
6 alkylheteroaryl moiety, or -N(R_C)₂, wherein each occurrence of R_C is independently hydrogen, a
7 protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl
8 moiety;

9 R₄ is hydrogen, halogen, cyano, -OR_D, -N(R_D)₂, -SR_D, -O(C=O)R_D, -N(R_D)(C=O)(R_D),
10 -C(O)R_D, -C(O)OR_D, -CON(R_D)₂, -OCO₂R_D, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
11 alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, a
12 protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl
13 moiety;

14 Z is O, S or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic,
15 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is
16 hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
17 alkylheteroaryl moiety;

18 X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

19 A and B together represent 

20 -CHR₅-CHR₆-, -CR₅=CR₆-, wherein R₅ and R₆ are each independently hydrogen, halogen,
21 cyano, -OR_J, -N(R_J)₂, -SR_J, -O(C=O)R_J, -O(S=O)R_J, -N(R_J)(C=O)(R_J), -C(=O)R_J, -C(=O)OR_J,
22 -CON(R_J)₂, -OCO₂R_J, -OS(=O)OR_J or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
23 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
24 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
25 wherein R₇ is hydrogen, a protecting group, -OR_K, -SR_K, -C(O)OR_K, -C(O)NR_K, -S(O)₂R_K, -
26 O(C=O)R_K, -N(R_K)(C=O)(R_K), -C(O)R_K, -C(O)OR_K, -CON(R_K)₂, -OCO₂R_K, or an aliphatic,
27 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
28 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
29 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent -CHR₅-

1 CHR₆-, R₅ and R₆ taken together represent a substituted or unsubstituted 3-7 membered aliphatic,
2 heteroaliphatic, aryl or heteroaryl ring;

3 D and E together represent -CHR₈-CHR₉-, -CR₈=CR₉-, wherein R₈ and R₉ are each
4 independently hydrogen or lower alkyl;

5 G and J together represent -CHR₁₀-CHR₁₁-, -CR₁₀=CR₁₁-, wherein R₁₀ and R₁₁ are each
6 independently hydrogen or lower alkyl;

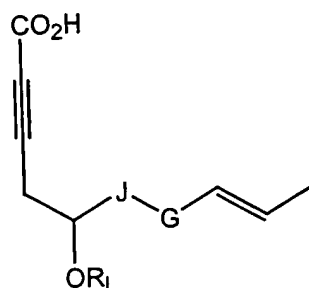
7 K and L together represent C=O, C=S, CH-CH₃, CH-CH(R_L)₂, C=C(R_L)₂, -CH₂-,
8 -C(-S(CH₂)₃S-)-, CH-OR_L, CH-SR_L, CH-N(R_L)₂, CH-N(R_L)(C=O)(R_L), C=N-O-R_L, CH-N=O,
9 C=C(R_L)-N(R_L)₂, C=N-R_L, C=N-N(R_L)₂, or, if the dotted line --- represents a bond, whereby a
10 double bond is present, then K and L together represent C-N(R_L)₂, wherein each occurrence of
11 R_L is independently hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl,
12 alkylaryl, or alkylheteroaryl moiety, or two occurrences of R_L taken together represent a 3 to 7-
13 membered cyclic aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

14 whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently
15 be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl,
16 heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted;
17 wherein one or any two of R₁, R_A, R₂, R_B, R₃, R_C, R₄, R_D, R₅, R₆, R_J, or R_L are optionally a linker
18 covalently bonded to a compound selected from the group consisting of radicicol, monocillin,
19 analogues of radicicol and monocillin, geldanamycin, analogues of geldanamycin, and steroids,

20 said method comprising:

21 (1) reacting an acidic component having the structure:

22

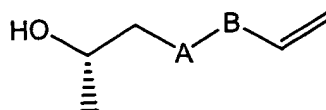


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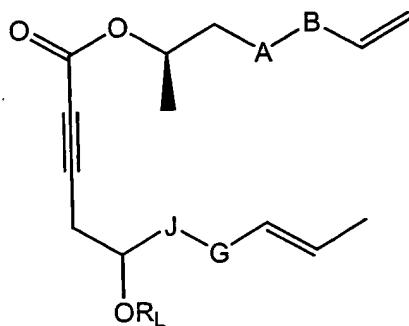
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wherein R_L, J, and G are as defined above, with a chiral component having the structure:

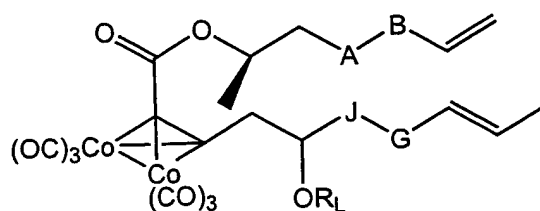
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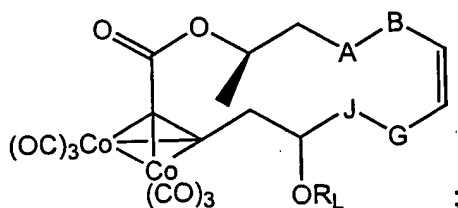
1 wherein A and B are as defined above, in the presence of an esterification reagent to
 2 generate an intermediate having the structure:



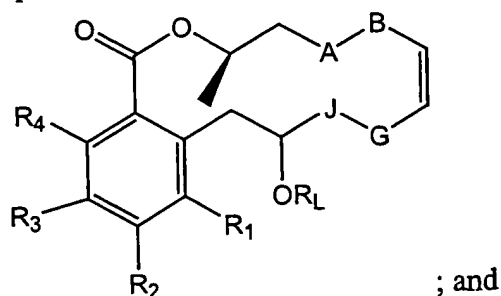
3
 4
 5 (2) complexing the intermediate with a cobalt, such as dicobalt hexacarbonyl, to yield a
 6 structure:



8
 9
 10 (3) cyclizing the cobalt complex in the presence of an olefin metathesis catalyst to
 11 generate the compound:



12
 13 (4) removing the cobalt to form a ynolide;
 14 (5) reacting the alkyne moiety of the ynolide with a diene under cycloaddition
 15 conditions to generate the compound:



(6) optionally further reacting the macrocycle with one or more reagents to diversify and optionally deprotecting the macrocycle to generate a compound having the formula (I).

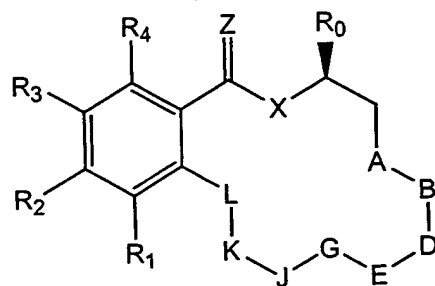
21. The method of claim 20, wherein the step of esterification is performed using diethylazodicarboxylate (DIAD) in the presence of triphenylphosphine or trifurylphosphine.

22. The method of claim 20, wherein the step of olefin metathesis is performed using an olefin metathesis catalyst.

23. The method of claim 20, wherein the step of olefin metathesis is performed using a ruthenium-based olefin metathesis catalyst.

24. The method of claim 23, wherein the step of olefin metathesis is performed using Ru(1,3-dimesityl-4,5-dihydro-imidazol-2-ylidene)(=CHCH=C(CH₃)₂)PCp₃Cl₂.

25. A method for synthesis of a macrocycle having the structure (IIa):



(IIa)

wherein

R₀ is hydrogen, halogen, cyano, -OR_Z, -N(R_Z)₂, -SR_Z, -O(C=O)R_Z, -N(R_Z)(C=O)(R_Z), -C(O)R_Z, -C(O)OR_Z, -CON(R_Z)₂, -OCO₂R_Z, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_Z is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety

R₁ is hydrogen, halogen, cyano, -OR_A, -N(R_A)₂, -SR_A, -O(C=O)R_A, -N(R_A)(C=O)(R_A), -C(O)R_A, -C(O)OR_A, -CON(R_A)₂, -OCO₂R_A, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_A is independently hydrogen, a

1 protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl
2 moiety;

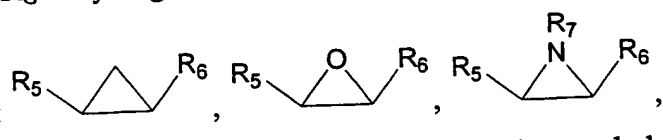
3 R_2 is hydrogen, halogen, cyano, $-OR_B$, $-N(R_B)_2$, $-SR_B$, $-O(C=O)R_B$, $-N(R_B)(C=O)(R_B)$,
4 $-C(O)R_B$, $-C(O)OR_B$, $-CON(R_B)_2$, $-OCO_2R_B$, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
5 alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_B is independently hydrogen, a
6 protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl
7 moiety;

8 R_3 is hydrogen, halogen, cyano, $-OR_C$, $-N(R_C)_2$, $-SR_C$, $-O(C=O)R_C$, $-N(R_C)(C=O)(R_C)$,
9 $-C(O)R_C$, $-C(O)OR_C$, $-CON(R_C)_2$, $-OCO_2R_C$, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
10 alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_C is independently hydrogen, a
11 protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl
12 moiety;

13 R_4 is hydrogen, halogen, cyano, $-OR_D$, $-N(R_D)_2$, $-SR_D$, $-O(C=O)R_D$, $-N(R_D)(C=O)(R_D)$,
14 $-C(O)R_D$, $-C(O)OR_D$, $-CON(R_D)_2$, $-OCO_2R_D$, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
15 alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, a
16 protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl
17 moiety;

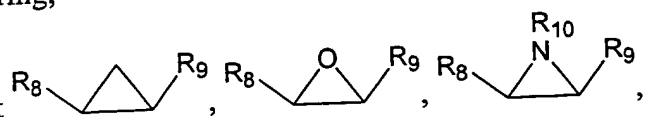
18 Z is O, S, or NR_E , wherein R_E is hydrogen, a protecting group, an aliphatic,
19 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F , wherein R_F is
20 hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
21 alkylheteroaryl moiety;

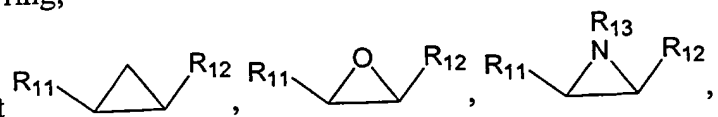
22 X is O, S or NR_G , wherein R_G is hydrogen or lower alkyl;

23 A and B together represent 

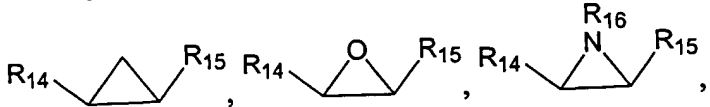
24 $-CHR_5-CHR_6-$, $-CR_5=CR_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen,
25 cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$, $-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,
26 $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
27 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
28 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
29 wherein R_7 is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$,
30 $O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic,

1 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
 2 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
 3 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-\text{CHR}_5-$
 4 CHR_6- , R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic,
 5 heteroaliphatic, aryl or heteroaryl ring;

6 D and E together represent ,
 7 $-\text{CHR}_8-\text{CHR}_9-$, $-\text{CR}_8=\text{CR}_9-$, wherein R_8 and R_9 are each independently hydrogen, halogen,
 8 cyano, $-\text{OR}_J$, $-\text{N}(\text{R}_J)_2$, $-\text{SR}_J$, $-\text{O}(\text{C}=\text{O})\text{R}_J$, $-\text{O}(\text{S}=\text{O})\text{R}_J$, $-\text{N}(\text{R}_J)(\text{C}=\text{O})(\text{R}_J)$, $-\text{C}(=\text{O})\text{R}_J$, $-\text{C}(=\text{O})\text{OR}_J$,
 9 $-\text{CON}(\text{R}_J)_2$, $-\text{OCO}_2\text{R}_J$, $-\text{OS}(=\text{O})\text{OR}_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
 10 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
 11 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
 12 wherein R_{10} is hydrogen, a protecting group, $-\text{OR}_K$, $-\text{SR}_K$, $-\text{C}(\text{O})\text{OR}_K$, $-\text{C}(\text{O})\text{NR}_K$, $-\text{S}(\text{O})_2\text{R}_K$,
 13 $\text{O}(\text{C}=\text{O})\text{R}_K$, $-\text{N}(\text{R}_K)(\text{C}=\text{O})(\text{R}_K)$, $-\text{C}(\text{O})\text{R}_K$, $-\text{C}(\text{O})\text{OR}_K$, $-\text{CON}(\text{R}_K)_2$, $-\text{OCO}_2\text{R}_K$, or an aliphatic,
 14 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of
 15 R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
 16 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-\text{CHR}_8-$
 17 CHR_9- , R_8 and R_9 taken together represent a substituted or unsubstituted 3-7 membered aliphatic,
 18 heteroaliphatic, aryl or heteroaryl ring;

19 G and J together represent ,
 20 $-\text{CHR}_{11}-\text{CHR}_{12}-$, $-\text{CR}_{11}=\text{CR}_{12}-$, wherein R_{11} and R_{12} are each independently hydrogen, halogen,
 21 cyano, $-\text{OR}_J$, $-\text{N}(\text{R}_J)_2$, $-\text{SR}_J$, $-\text{O}(\text{C}=\text{O})\text{R}_J$, $-\text{O}(\text{S}=\text{O})\text{R}_J$, $-\text{N}(\text{R}_J)(\text{C}=\text{O})(\text{R}_J)$, $-\text{C}(=\text{O})\text{R}_J$, $-\text{C}(=\text{O})\text{OR}_J$,
 22 $-\text{CON}(\text{R}_J)_2$, $-\text{OCO}_2\text{R}_J$, $-\text{OS}(=\text{O})\text{OR}_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
 23 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
 24 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
 25 wherein R_{13} is hydrogen, a protecting group, $-\text{OR}_K$, $-\text{SR}_K$, $-\text{C}(\text{O})\text{OR}_K$, $-\text{C}(\text{O})\text{NR}_K$, $-\text{S}(\text{O})_2\text{R}_K$,
 26 $\text{O}(\text{C}=\text{O})\text{R}_K$, $-\text{N}(\text{R}_K)(\text{C}=\text{O})(\text{R}_K)$, $-\text{C}(\text{O})\text{R}_K$, $-\text{C}(\text{O})\text{OR}_K$, $-\text{CON}(\text{R}_K)_2$, $-\text{OCO}_2\text{R}_K$, or an aliphatic,
 27 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
 28 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
 29 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-\text{CHR}_{11}-$

1 CHR₁₂-, R₁₁ and R₁₂ taken together represent a substituted or unsubstituted 3-7 membered
2 aliphatic, heteroaliphatic, aryl or heteroaryl ring;

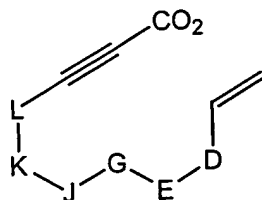
3 K and L together represent ,
4 -CHR₁₄-CHR₁₅-, -CR₁₄=CR₁₅-, wherein R₁₄ and R₁₅ are each independently hydrogen, halogen,
5 cyano, -OR_J, -N(R_J)₂, -SR_J, -O(C=O)R_J, -O(S=O)R_J, -N(R_J)(C=O)(R_J), -C(=O)R_J, -C(=O)OR_J,
6 -CON(R_J)₂, -OCO₂R_J, -OS(=O)OR_J or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
7 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
8 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
9 wherein R₁₆ is hydrogen, a protecting group, -OR_K, -SR_K, -C(O)OR_K, -C(O)NR_K, -S(O)₂R_K, -
10 O(C=O)R_K, -N(R_K)(C=O)(R_K), -C(O)R_K, -C(O)OR_K, -CON(R_K)₂, -OCO₂R_K, or an aliphatic,
11 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
12 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
13 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent -CHR₁₄-
14 CHR₁₅-, R₁₄ and R₁₅ taken together represent a substituted or unsubstituted 3-7 membered
15 aliphatic, heteroaliphatic, aryl or heteroaryl ring;

16 whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently
17 be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl,
18 heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted,

19 said method comprising:

20 (1) reacting a component having the structure:

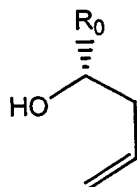
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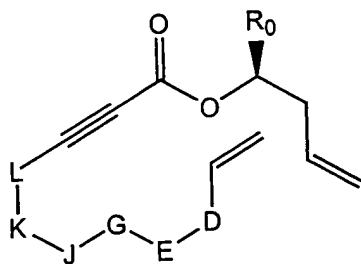
23

wherein R_L, J, and G are as defined above, with a chiral component having the structure:

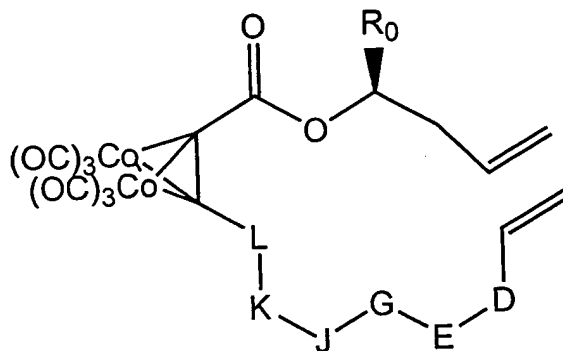


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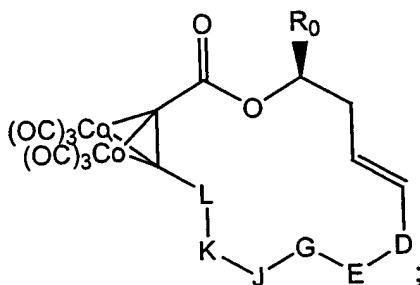
1 wherein A, B, D, E, G, J, K, and L are as defined above, in the presence of an
 2 esterification reagent to generate an intermediate having the structure:



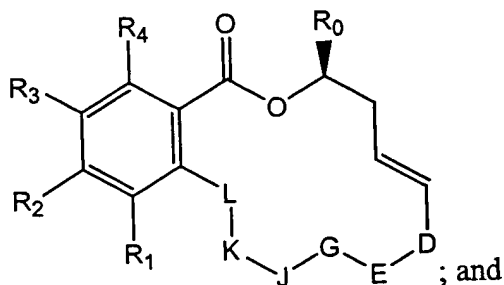
3
 4
 5 (2) complexing the intermediate with a cobalt, such as dicobalt hexacarbonyl, to yield a
 6 structure:



7
 8
 9 (3) cyclizing the cobalt complex in the presence of an olefin metathesis catalyst to
 10 generate the compound:



11
 12 (4) removing the cobalt to form a ynolide;
 13 (5) reacting the alkyne moiety of the ynolide with a diene under cycloaddition
 14 conditions to generate the compound:



(6) optionally further reacting the macrocycle with one or more reagents to diversify and optionally deprotecting the macrocycle to generate a compound having the formula (IIa).

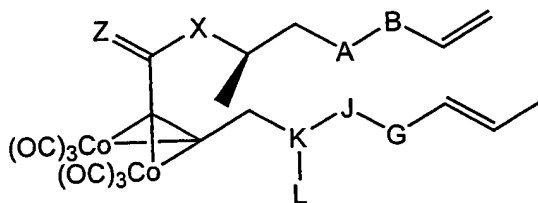
26. The method of claim 25, wherein the method further comprises further diversifying the macrocycle to generate a compound having the structure (II) as defined herein.

27. The method of claim 25, wherein the step of olefin metathesis is performed using an olefin metathesis catalyst.

28. The method of claim 25, wherein the step of olefin metathesis is performed using a ruthenium-based olefin metathesis catalyst.

29. The method of claim 28, wherein the step of olefin metathesis is performed using Ru(1,3-dimesityl-4,5-dihydro-imidazol-2-ylidene)(=CHCH=C(CH₃)₂)PCp₃Cl₂.

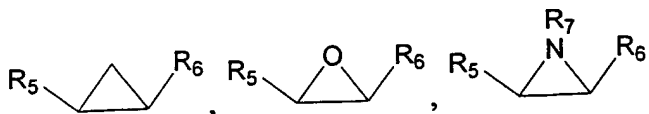
30. A compound of the formula:



wherein

Z is O, S or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;



A and B together represent

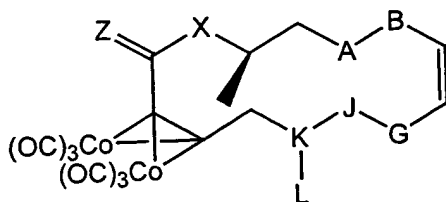
-CHR₅-CHR₆-, -CR₅=CR₆-, wherein R₅ and R₆ are each independently hydrogen, halogen, cyano, -OR_J, -N(R_J)₂, -SR_J, -O(C=O)R_J, -O(S=O)R_J, -N(R_J)(C=O)(R_J), -C(=O)R_J, -C(=O)OR_J, -CON(R_J)₂, -OCO₂R_J, -OS(=O)OR_J or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R₇ is hydrogen, a protecting group, -OR_K, -SR_K, -C(O)OR_K, -C(O)NR_K, -S(O)₂R_K, -O(C=O)R_K, -N(R_K)(C=O)(R_K), -C(O)R_K, -C(O)OR_K, -CON(R_K)₂, -OCO₂R_K, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent -CHR₅-CHR₆-, R₅ and R₆ taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring,

G and J together represent -CHR₁₀-CHR₁₁-, -CR₁₀=CR₁₁-, wherein R₁₀ and R₁₁ are each independently hydrogen or lower alkyl;

K and L together represent C=O, C=S, CH-CH₃, CH-CH(R_L)₂, C=C(R_L)₂, -CH₂-, -C(-S(CH₂)₃S-), CH-OR_L, CH-SR_L, CH-N(R_L)₂, CH-N(R_L)(C=O)(R_L), C=N-O-R_L, CH-N=O, C=C(R_L)-N(R_L)₂, C=N-R_L, C=N-N(R_L)₂, or, if the dotted line --- represents a bond, whereby a double bond is present, then K and L together represent C-N(R_L)₂, wherein each occurrence of R_L is independently hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or two occurrences of R_L taken together represent a 3 to 7-membered cyclic aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl, heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted; wherein one or any two of R_A, R_B, R_C, R_D, R₅, R₆, R_J, or R_L are optionally a linker covalently bonded to a compound selected from the group consisting of radicicol, monocillin, analogues of radicicol and monocillin, geldanamycin, analogues of geldanamycin, and steroids.

31. A compound of the formula:

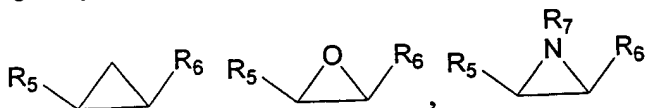


wherein

Z is O, S or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

X is O, S or NR_G, wherein R_G is hydrogen or lower alkyl;

A and B together represent



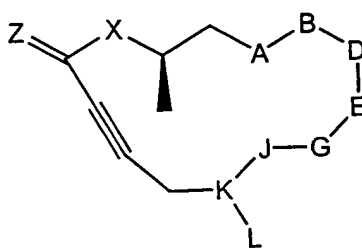
-CHR₅-CHR₆-, -CR₅=CR₆-, wherein R₅ and R₆ are each independently hydrogen, halogen, cyano, -OR_J, -N(R_J)₂, -SR_J, -O(C=O)R_J, -O(S=O)R_J, -N(R_J)(C=O)(R_J), -C(=O)R_J, -C(=O)OR_J, -CON(R_J)₂, -OCO₂R_J, -OS(=O)OR_J or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R₇ is hydrogen, a protecting group, -OR_K, -SR_K, -C(O)OR_K, -C(O)NR_K, -S(O)₂R_K, -O(C=O)R_K, -N(R_K)(C=O)(R_K), -C(O)R_K, -C(O)OR_K, -CON(R_K)₂, -OCO₂R_K, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent -CHR₅-CHR₆-, R₅ and R₆ taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring,

G and J together represent -CHR₁₀-CHR₁₁-, -CR₁₀=CR₁₁-, wherein R₁₀ and R₁₁ are each independently hydrogen or lower alkyl;

K and L together represent C=O, C=S, CH-CH₃, CH-CH(R_L)₂, C=C(R_L)₂, -CH₂-, -C(-S(CH₂)₃S-)-, CH-OR_L, CH-SR_L, CH-N(R_L)₂, CH-N(R_L)(C=O)(R_L), C=N-O-R_L, CH-N=O, C=C(R_L)-N(R_L)₂, C=N-R_L, C=N-N(R_L)₂, or, if the dotted line --- represents a bond, whereby a double bond is present, then K and L together represent C-N(R_L)₂, wherein each occurrence of R_L is independently hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl,

1 alkylaryl, or alkylheteroaryl moiety, or two occurrences of R_L taken together represent a 3 to 7-
 2 membered cyclic aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;
 3 whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently
 4 be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl,
 5 heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted;
 6 wherein one or any two of R_A , R_B , R_C , R_D , R_5 , R_6 , R_J , or R_L are optionally a linker covalently
 7 bonded to a compound selected from the group consisting of radicicol, monocillin, analogues of
 8 radicicol and monocillin, geldanamycin, analogues of geldanamycin, and steroids.

9
 10 32. A compound of the formula:



11
 12 wherein
 13 Z is O, S or NR_E , wherein R_E is hydrogen, a protecting group, an aliphatic,
 14 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F , wherein R_F is
 15 hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
 16 alkylheteroaryl moiety;

17 X is O, S or NR_G , wherein R_G is hydrogen or lower alkyl;

18 A and B together represent ,
 19 $-CHR_5-CHR_6-$, $-CR_5=CR_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen,
 20 cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$, $-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,
 21 $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
 22 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
 23 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
 24 wherein R_7 is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-$
 25 $O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic,
 26 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence

1 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
2 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-\text{CHR}_5-$
3 CHR_6- , R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic,
4 heteroaliphatic, aryl or heteroaryl ring;

5 D and E together represent $-\text{CHR}_8-\text{CHR}_9-$, $-\text{CR}_8=\text{CR}_9-$, wherein R_8 and R_9 are each
6 independently hydrogen or lower alkyl;

7 G and J together represent $-\text{CHR}_{10}-\text{CHR}_{11}-$, $-\text{CR}_{10}=\text{CR}_{11}-$, wherein R_{10} and R_{11} are each
8 independently hydrogen or lower alkyl;

9 K and L together represent $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{CH}-\text{CH}_3$, $\text{CH}-\text{CH}(\text{R}_L)_2$, $\text{C}=\text{C}(\text{R}_L)_2$, $-\text{CH}_2-$,
10 $-\text{C}(\text{S}(\text{CH}_2)_3\text{S}-)$, $\text{CH}-\text{OR}_L$, $\text{CH}-\text{SR}_L$, $\text{CH}-\text{N}(\text{R}_L)_2$, $\text{CH}-\text{N}(\text{R}_L)(\text{C}=\text{O})(\text{R}_L)$, $\text{C}=\text{N}-\text{O}-\text{R}_L$, $\text{CH}-\text{N}=\text{O}$,
11 $\text{C}=\text{C}(\text{R}_L)-\text{N}(\text{R}_L)_2$, $\text{C}=\text{N}-\text{R}_L$, $\text{C}=\text{N}-\text{N}(\text{R}_L)_2$, or, if the dotted line --- represents a bond, whereby a
12 double bond is present, then K and L together represent $\text{C}-\text{N}(\text{R}_L)_2$, wherein each occurrence of
13 R_L is independently hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl,
14 alkylaryl, or alkylheteroaryl moiety, or two occurrences of R_L taken together represent a 3 to 7-
15 membered cyclic aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

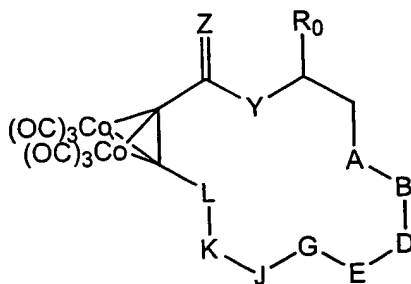
16 whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently
17 be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl,
18 heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted;
19 wherein one or any two of R_A , R_B , R_C , R_D , R_5 , R_6 , R_J , or R_L are optionally a linker covalently
20 bonded to a compound selected from the group consisting of radicicol, monocillin, analogues of
21 radicicol and monocillin, geldanamycin, analogues of geldanamycin, and steroids.

22

23 33. The compound of claim 32, wherein D and E together represent $-\text{CR}_8=\text{CR}_9-$.

24

25 34. A compound of formula:

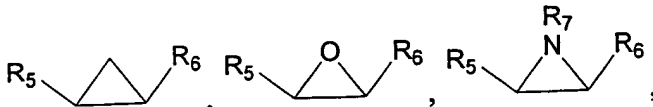



26

27 wherein

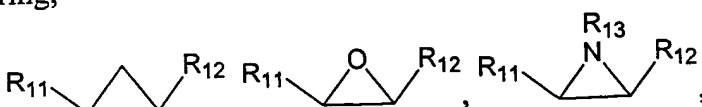
1 R_0 is hydrogen, cyano, $-OR_Z$, $-N(R_Z)_2$, $-SR_Z$, $-O(C=O)R_Z$, $-N(R_Z)(C=O)(R_Z)$, $-C(O)R_Z$, $-$
2 $C(O)OR_Z$, $-CON(R_Z)_2$, $-OCO_2R_Z$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
3 alkylheteroaryl moiety, wherein each occurrence of R_Z is independently hydrogen, a protecting
4 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety
5 Z is O, S, or NR_E , wherein R_E is hydrogen, a protecting group, an aliphatic,
6 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F , wherein R_F is
7 hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
8 alkylheteroaryl moiety;

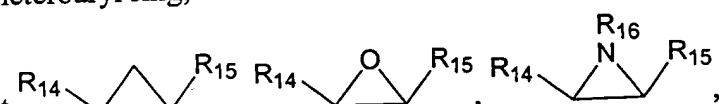
9 X is O, S or NR_G , wherein R_G is hydrogen or lower alkyl;

10 A and B together represent ,
11 $-CHR_5-CHR_6-$, $-CR_5=CR_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen,
12 cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$, $-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,
13 $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
14 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
15 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
16 wherein R_7 is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-$
17 $O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic,
18 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
19 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
20 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_5-$
21 CHR_6- , R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic,
22 heteroaliphatic, aryl or heteroaryl ring;

23 D and E together represent ,
24 $-CHR_8-CHR_9-$, $-CR_8=CR_9-$, wherein R_8 and R_9 are each independently hydrogen, halogen,
25 cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$, $-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,
26 $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
27 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
28 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
29 wherein R_{10} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-$

1 $O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic,
2 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of
3 R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
4 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_8-$
5 CHR_9- , R_9 and R_9 taken together represent a substituted or unsubstituted 3-7 membered aliphatic,
6 heteroaliphatic, aryl or heteroaryl ring;

7 G and J together represent ,
8 $-CHR_{11}-CHR_{12}-$, $-CR_{11}=CR_{12}-$, wherein R_{11} and R_{12} are each independently hydrogen, halogen,
9 cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$, $-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,
10 $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
11 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
12 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
13 wherein R_{13} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$,
14 $O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic,
15 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
16 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
17 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{11}-$
18 $CHR_{12}-$, R_{11} and R_{12} taken together represent a substituted or unsubstituted 3-7 membered
19 aliphatic, heteroaliphatic, aryl or heteroaryl ring;

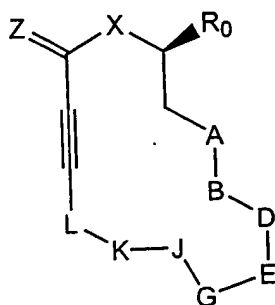
20 K and L together represent ,
21 $-CHR_{14}-CHR_{15}-$, $-CR_{14}=CR_{15}-$, wherein R_{14} and R_{15} are each independently hydrogen, halogen,
22 cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$, $-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,
23 $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
24 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
25 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
26 wherein R_{16} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$,
27 $O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic,
28 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
29 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,

1 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-\text{CHR}_{14}-$
 2 $\text{CHR}_{15}-$, R_{14} and R_{15} taken together represent a substituted or unsubstituted 3-7 membered
 3 aliphatic, heteroaliphatic, aryl or heteroaryl ring;

4 whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently
 5 be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl,
 6 heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted.

7
 8 35. The compound of claim 34, wherein A and B together represent $-\text{CR}_5=\text{CR}_6-$.

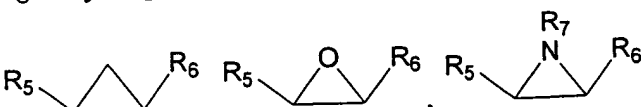
9
 10 36. A compound of the formula:



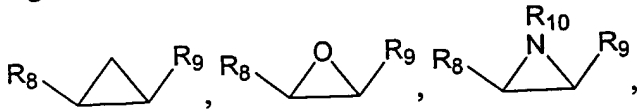
11
 12 wherein
 13 R_0 is hydrogen, cyano, $-\text{OR}_Z$, $-\text{N}(\text{R}_Z)_2$, $-\text{SR}_Z$, $-\text{O}(\text{C}=\text{O})\text{R}_Z$, $-\text{N}(\text{R}_Z)(\text{C}=\text{O})(\text{R}_Z)$, $-\text{C}(\text{O})\text{R}_Z$, $-\text{C}(\text{O})\text{OR}_Z$, $-\text{CON}(\text{R}_Z)_2$, $-\text{OCO}_2\text{R}_Z$, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
 14 alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_Z is independently hydrogen, a
 15 protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl
 16 moiety

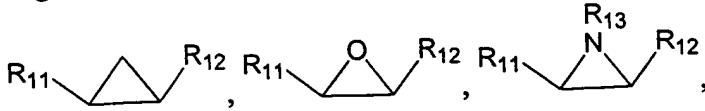
17
 18 Z is O, S, or NR_E , wherein R_E is hydrogen, a protecting group, an aliphatic,
 19 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F , wherein R_F is
 20 hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
 21 alkylheteroaryl moiety;

22 X is O, S or NR_G , wherein R_G is hydrogen or lower alkyl;

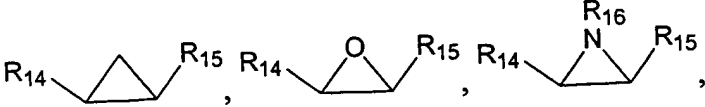
23 A and B together represent ,
 24 $-\text{CHR}_5-\text{CHR}_6-$, $-\text{CR}_5=\text{CR}_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen,
 25 cyano, $-\text{OR}_J$, $-\text{N}(\text{R}_J)_2$, $-\text{SR}_J$, $-\text{O}(\text{C}=\text{O})\text{R}_J$, $-\text{O}(\text{S}=\text{O})\text{R}_J$, $-\text{N}(\text{R}_J)(\text{C}=\text{O})(\text{R}_J)$, $-\text{C}(=\text{O})\text{R}_J$, $-\text{C}(=\text{O})\text{OR}_J$,

1 -CON(R_J)₂, -OCO₂R_J, -OS(=O)OR_J or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
 2 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
 3 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
 4 wherein R₇ is hydrogen, a protecting group, -OR_K, -SR_K, -C(O)OR_K, -C(O)NR_K, -S(O)₂R_K, -
 5 O(C=O)R_K, -N(R_K)(C=O)(R_K), -C(O)R_K, -C(O)OR_K, -CON(R_K)₂, -OCO₂R_K, or an aliphatic,
 6 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
 7 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
 8 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent -CHR₅-
 9 CHR₆-, R₅ and R₆ taken together represent a substituted or unsubstituted 3-7 membered aliphatic,
 10 heteroaliphatic, aryl or heteroaryl ring;

11 D and E together represent ,
 12 -CHR₈-CHR₉-, -CR₈=CR₉-, wherein R₈ and R₉ are each independently hydrogen, halogen,
 13 cyano, -OR_J, -N(R_J)₂, -SR_J, -O(C=O)R_J, -O(S=O)R_J, -N(R_J)(C=O)(R_J), -C(=O)R_J, -C(=O)OR_J,
 14 -CON(R_J)₂, -OCO₂R_J, -OS(=O)OR_J or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
 15 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
 16 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
 17 wherein R₁₀ is hydrogen, a protecting group, -OR_K, -SR_K, -C(O)OR_K, -C(O)NR_K, -S(O)₂R_K, -
 18 O(C=O)R_K, -N(R_K)(C=O)(R_K), -C(O)R_K, -C(O)OR_K, -CON(R_K)₂, -OCO₂R_K, or an aliphatic,
 19 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of
 20 R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
 21 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent -CHR₈-
 22 CHR₉-, R₉ and R₉ taken together represent a substituted or unsubstituted 3-7 membered aliphatic,
 23 heteroaliphatic, aryl or heteroaryl ring;

24 G and J together represent ,
 25 -CHR₁₁-CHR₁₂-, -CR₁₁=CR₁₂-, wherein R₁₁ and R₁₂ are each independently hydrogen, halogen,
 26 cyano, -OR_J, -N(R_J)₂, -SR_J, -O(C=O)R_J, -O(S=O)R_J, -N(R_J)(C=O)(R_J), -C(=O)R_J, -C(=O)OR_J,
 27 -CON(R_J)₂, -OCO₂R_J, -OS(=O)OR_J or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
 28 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
 29 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and

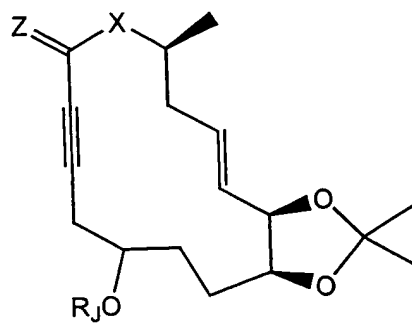
1 wherein R_{13} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-$
2 $O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic,
3 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
4 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
5 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{11}-$
6 $CHR_{12}-$, R_{11} and R_{12} taken together represent a substituted or unsubstituted 3-7 membered
7 aliphatic, heteroaliphatic, aryl or heteroaryl ring;

8 K and L together represent ,
9 $-CHR_{14}-CHR_{15}-$, $-CR_{14}=CR_{15}-$, wherein R_{14} and R_{15} are each independently hydrogen, halogen,
10 cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$, $-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$,
11 $-CON(R_J)_2$, $-OCO_2R_J$, $-OS(=O)OR_J$ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or
12 alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, a protecting
13 group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and
14 wherein R_{16} is hydrogen, a protecting group, $-OR_K$, $-SR_K$, $-C(O)OR_K$, $-C(O)NR_K$, $-S(O)_2R_K$, $-$
15 $O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic,
16 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence
17 of R_K is independently hydrogen, a protecting group or an aliphatic, heteroaliphatic, aryl,
18 heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_{14}-$
19 $CHR_{15}-$, R_{14} and R_{15} taken together represent a substituted or unsubstituted 3-7 membered
20 aliphatic, heteroaliphatic, aryl or heteroaryl ring;

21 whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently
22 be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl,
23 heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted.

24
25 37. The compound of claim 36, wherein A and B together represent $-CR_5=CR_6-$.

26
27 38. The compound of claim 36, wherein the compound has the formula:



1
2
3